

FIG. 1A

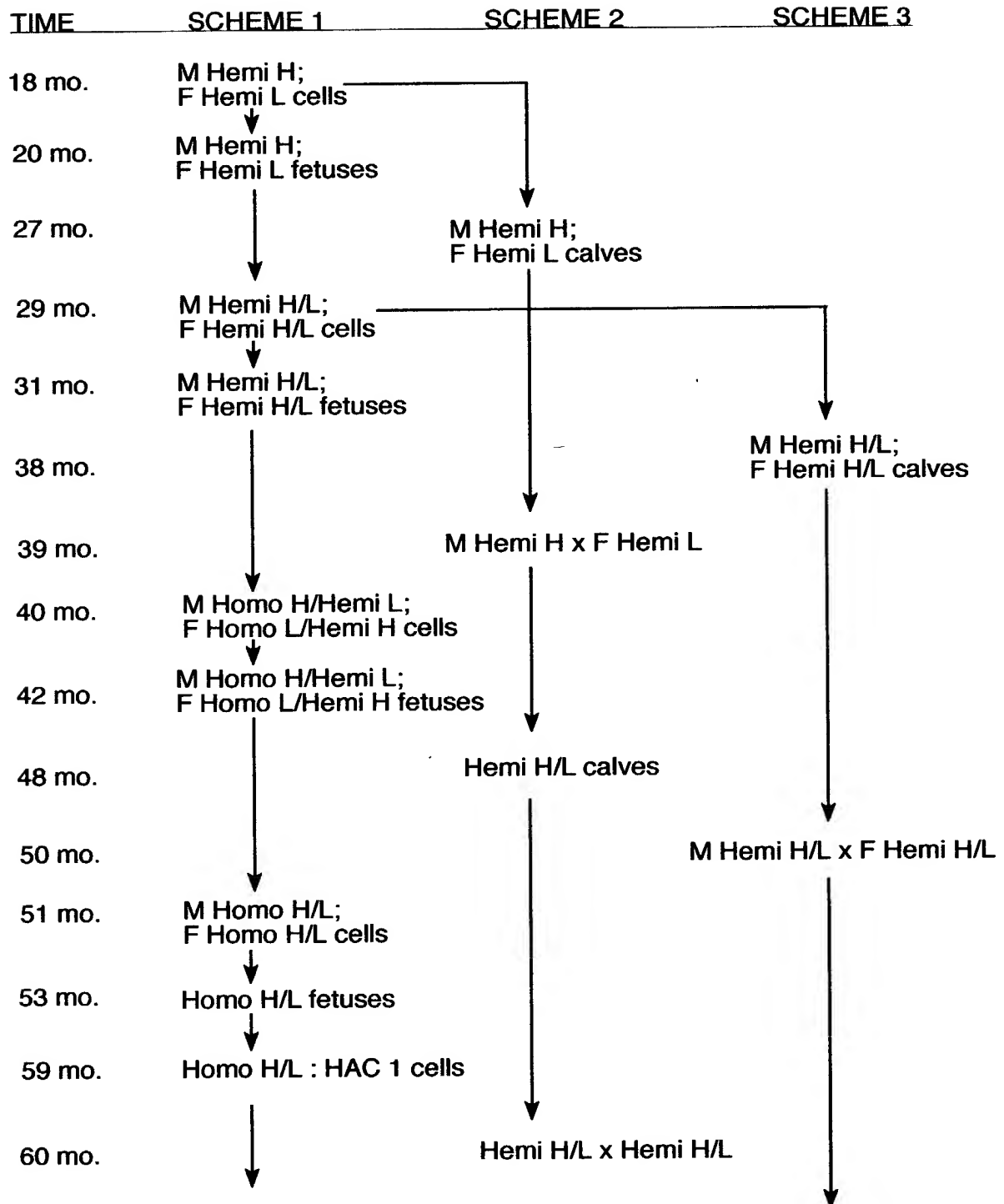


FIG. 1A (CONT.)

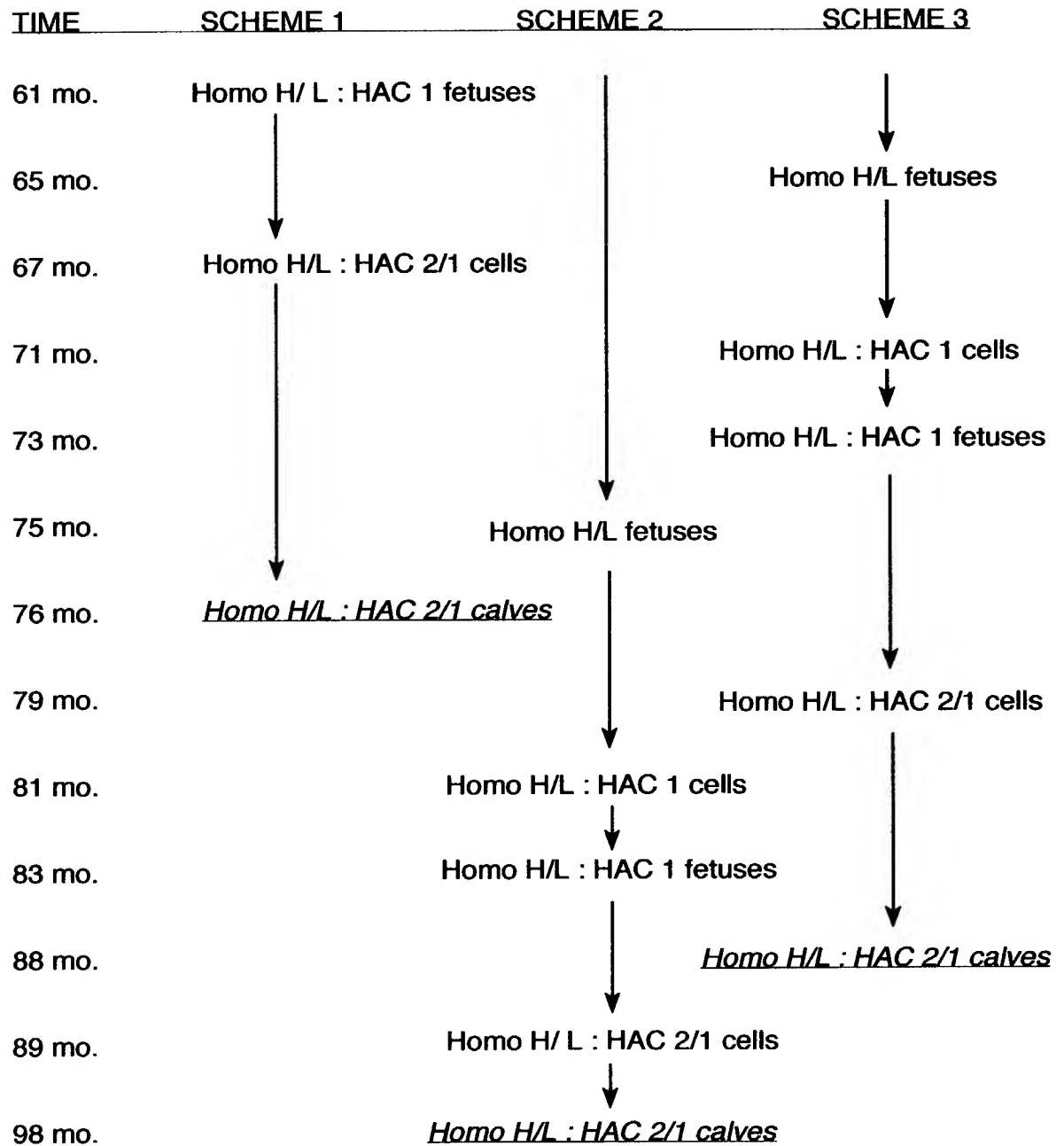


FIG. 1B

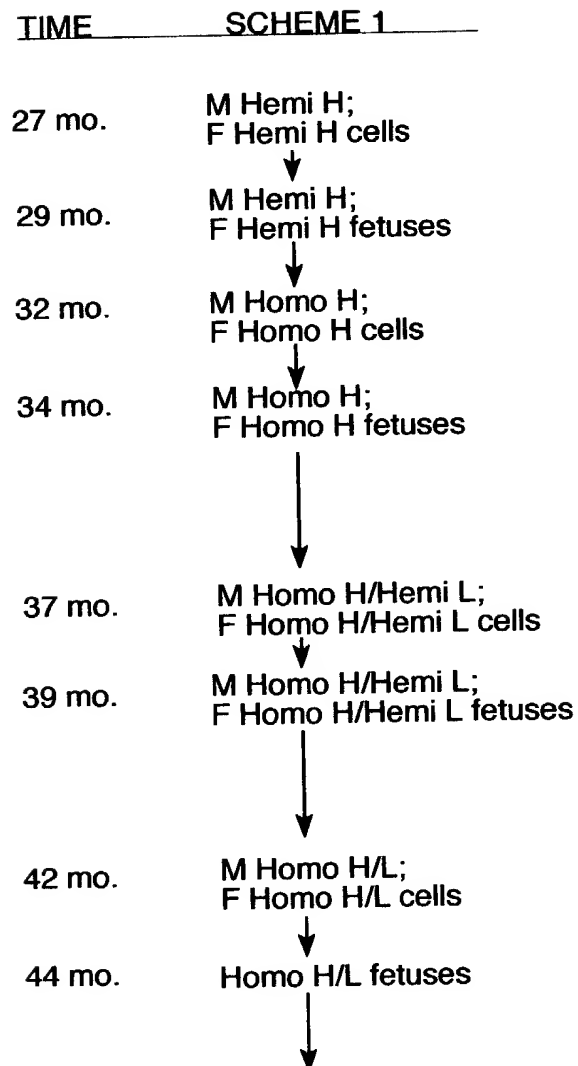


FIG. 1B (CONT.)

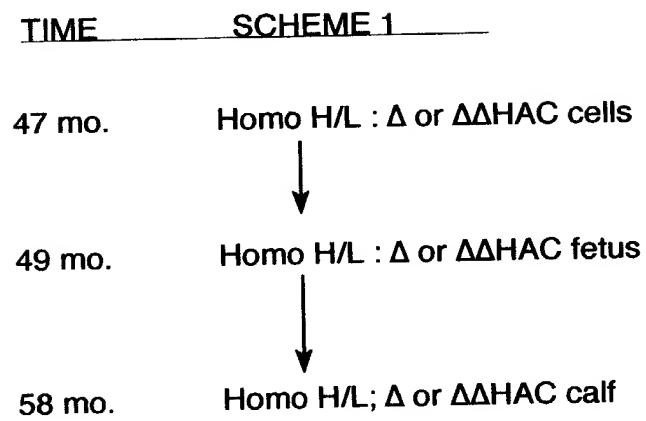


FIG. 2B

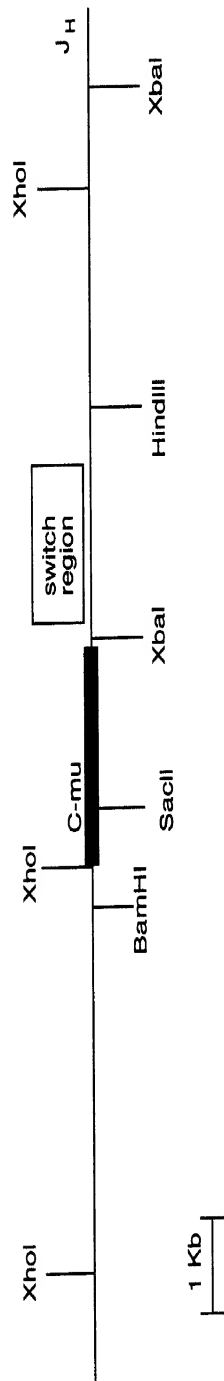


FIG. 2A

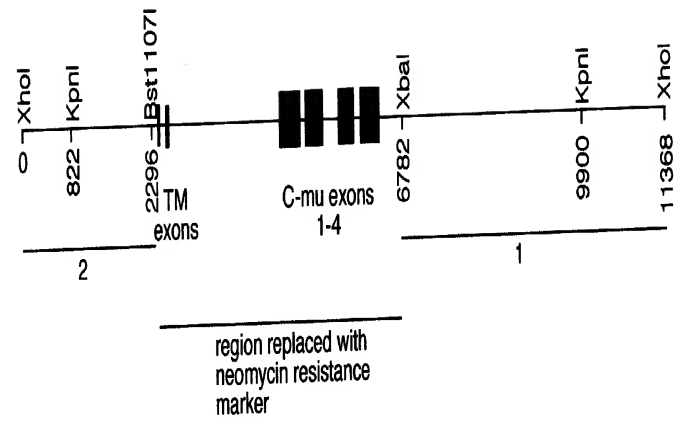


FIG. 2A

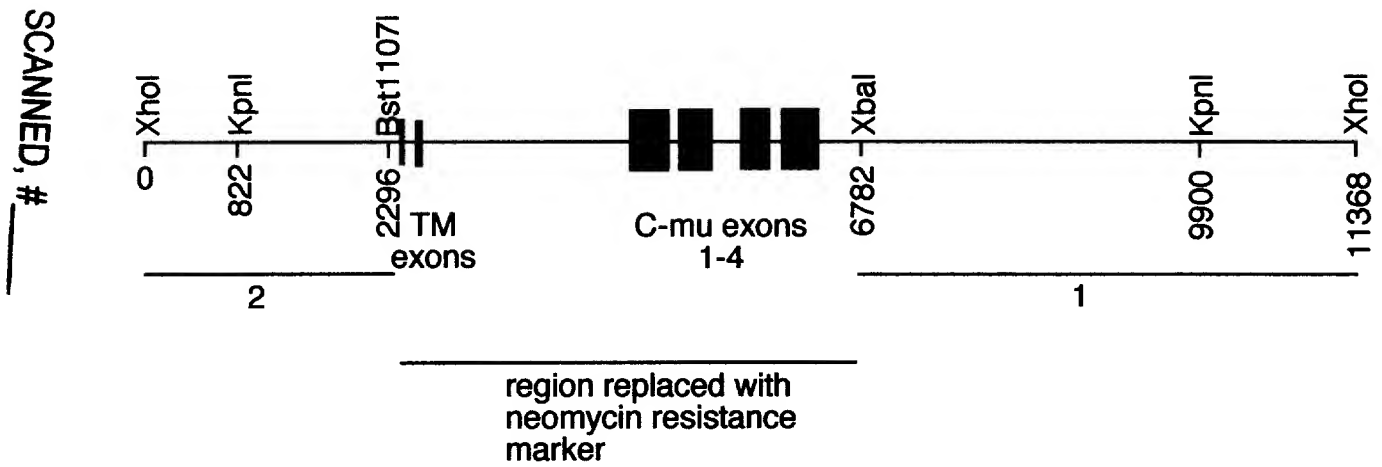


FIG. 2B

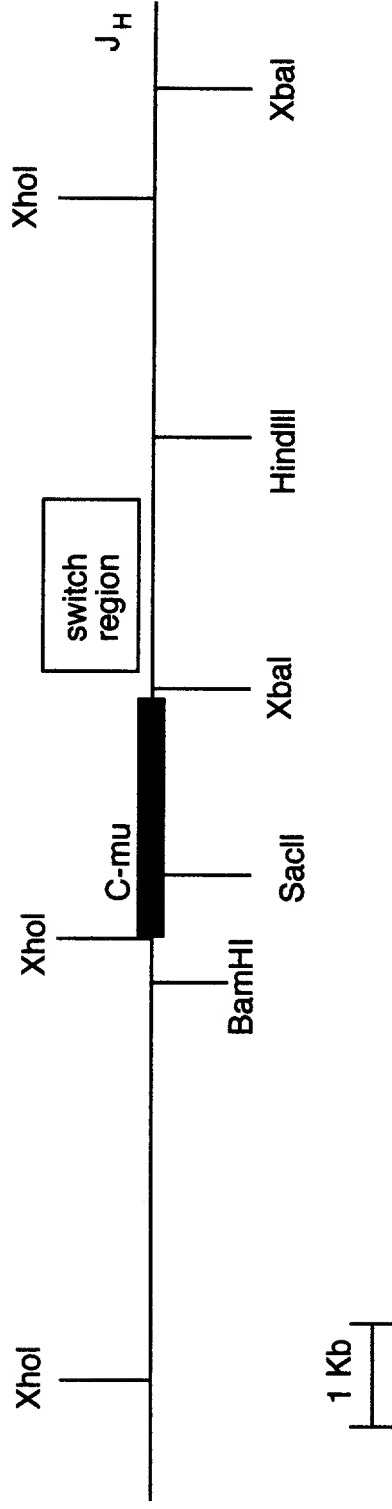


FIG. 3A

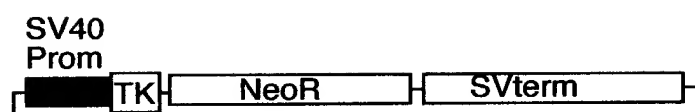


FIG. 3B

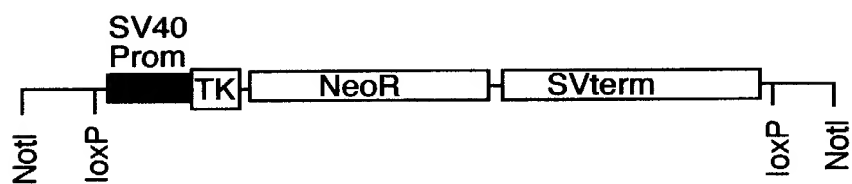
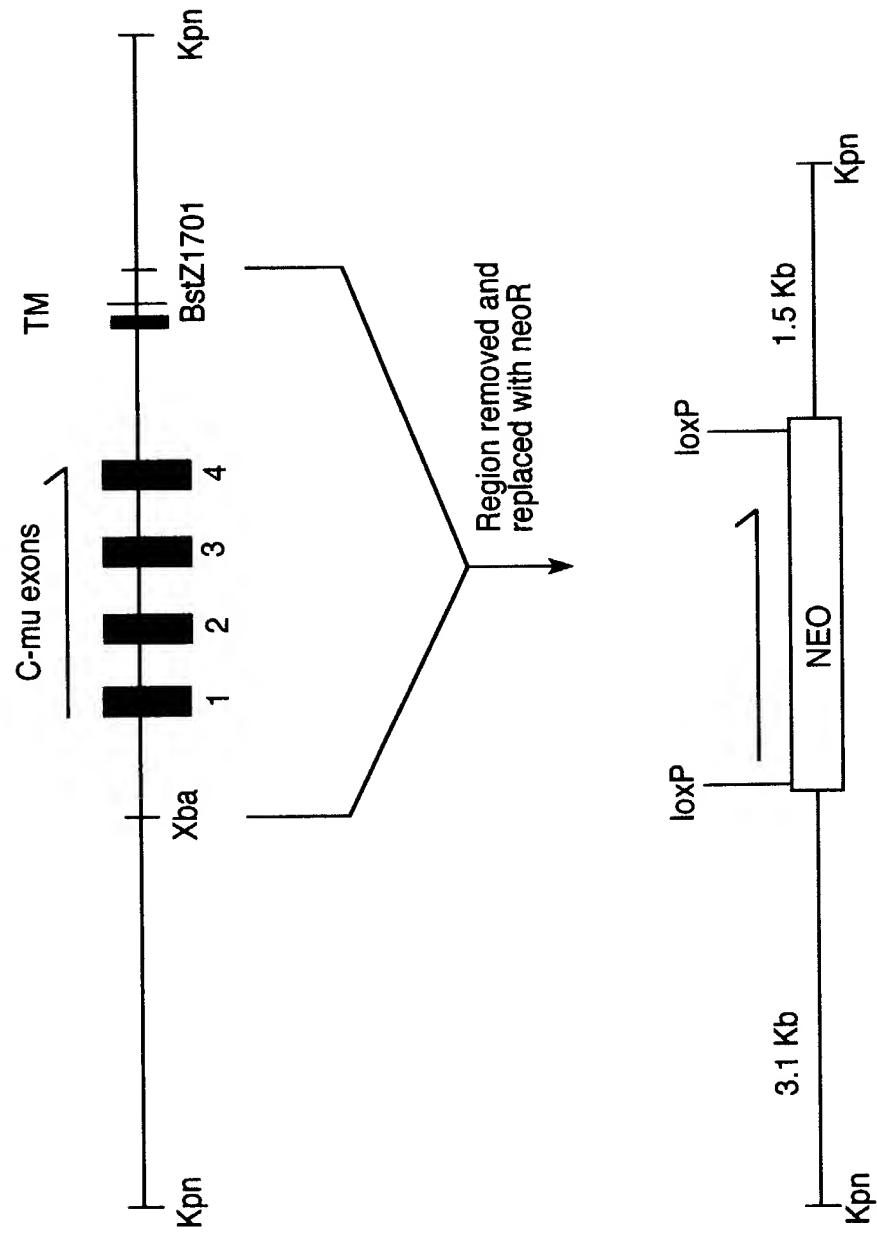


FIG. 3C



09988415, 060602

FIG. 3D

SEQ ID NO:47

ggtaccgaaaggcggccctgaacattctgcagtgagggagccgcactgagaaagctgcttcacgccgggagggagccagc
cagctacgattgtgagcacgctcacagtgcacacggcatgtgcacggctcagcttaaccacctgaaggagtaactcattaaag
agcgtacgaatgcattgataaaatgcacctgagacaaattaatttctaaacatcgactttgaaaatgaatataagtgagcagttgat
aggctctgaatgaaataccttccaacaggtgctgagaaccgccaggagcagggaaacggactccccgtggagccccagaagg
agccagccctgatgatacctcggccctgggccctcctcacgctgggagagagccagctcctgtgttcacgctggcctgtggtt
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cctcacccagctccctccccctggccccagggctcctcctccatcccaccgcccaccctaccctggcgttgcctgcacagctaa
cctgacctccctgggttcgagcgtgccgcccgcctcctgggccccacctggacccccgcagcctatctctgagggcctaagc
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aggccaccttgggaaaccagtcctgggatctgcaactcggccatgttccctgcatctggaccagccccaagacaccacccggc
gtgggccactggcctgggaggagacacatgtccttcccatcagcaatgggttcagcactaggtatgcagcacacaggag
tgtggcttgggggtaaaaaaaccttcacgaggaagcgggttcacaaaataaagta

FIG. 3E

FIG. 3F

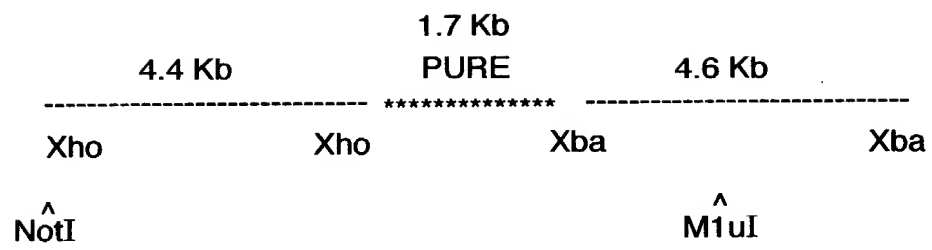


FIG. 3G

SEQ ID NO: 60

1 atgagattcc ctgctcagct cctggggctc ctctgctct gggccccagg
 51 atccagtggg gatgttggtc tgaccagac tcccctctcc ctgtctatca
 101 tccctggaga gacggtctcc atctctgca agtctactca gagtctgaaa
 151 tatagtgatg gaaaaaccta ttgtactgg cttaacata aaccaggcca
 201 atcaccacag cttttgatct atgctgttc cagccgttac actggggctc
 251 cagacaggtt cactggcagt gggtcagaaa cagattcac acttacgac
 301 aacagtgtgc aggctgagga tgttgagtc tattactgtc ttcaacaac
 351 atatgtcca aatactttcg gccaaggaac caaggtagag atcaaaaggt
 401 ctgatgtga gccatccgtc ttctcttca aaccatctga tgagcagctg
 451 aagaccggaa ctgtctctgt cgtgtgcttg gtgaatgatt tctacccaa
 501 agatatcaat gtcaagtgga aagtggatgg ggttactcag agcagcagca
 551 acttcaaaaa cagtttcaca gaccaggaca gcaagaaaag cacctacagc
 601 ctgagcagca tctgacact gccagctca gactacaaa gccatgacgc
 651 ctatacgtgt gaggtcagcc acaagagcct gactaccacc ctgtcaaga
 701 gcttcagtaa gaacgagtgt tag

FIG. 4

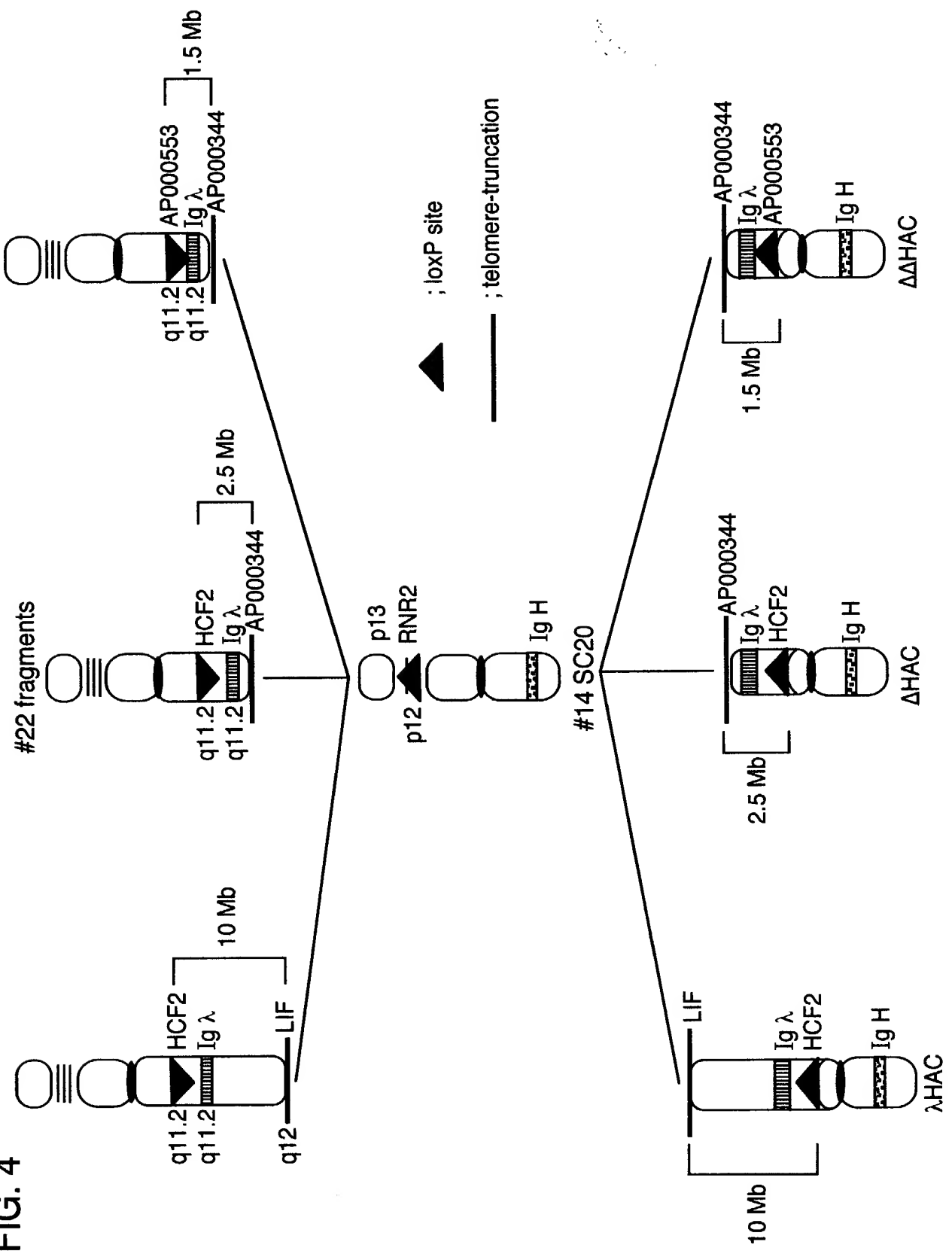
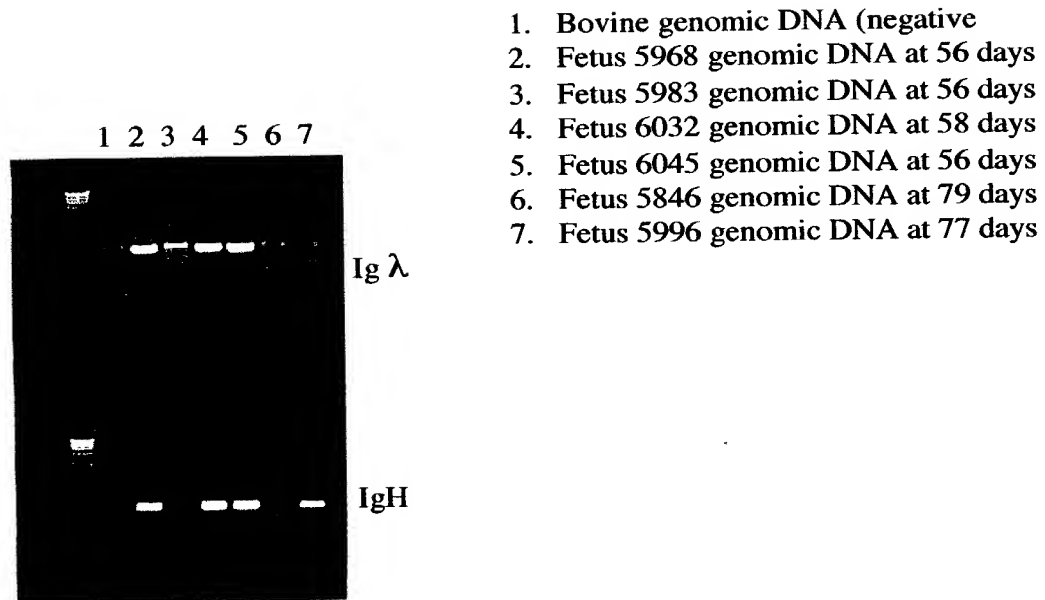
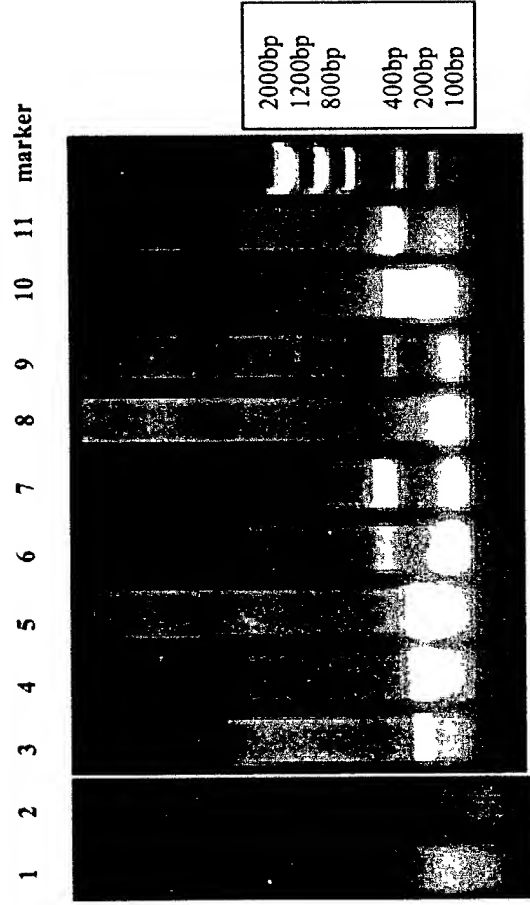


FIG. 5



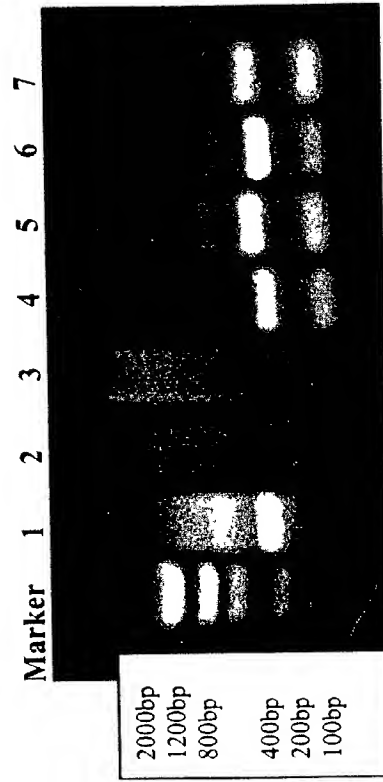
Fetus	Clone	IgH	Ig λ
5968	B4-2	Pos	Pos
5983	B2-13	Neg	Neg
6032	B4-8	Pos	Pos
6045	B2-22	Pos	Pos
5846	B4-8	Neg	Neg
5996	B4-2	Pos	Neg

FIG. 6



1. Human mu constant region in bovine liver cDNA from fetus 5996.
2. Human mu constant region in bovine brain cDNA from fetus 5996.
3. Human mu constant region in bovine spleen cDNA from fetus 5996.
4. Human mu constant region in human spleen cDNA.
5. Human mu constant region in mouse spleen cDNA with HAC.
6. Bovine rearranged Cmu heavy chain in bovine spleen cDNA from fetus 5996.
7. Bovine rearranged Cmu heavy chain in human spleen cDNA.
8. Bovine rearranged Cmu heavy chain in mouse spleen cDNA with HAC.
9. GAPDH primers in bovine spleen cDNA from fetus 5996.
10. GAPDH primers in bovine liver cDNA
11. GAPDH primers in mouse spleen cDNA with HAC.

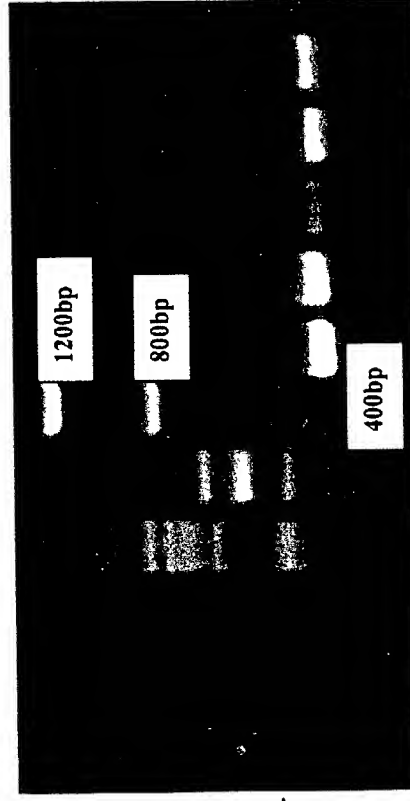
FIG. 7



1. GAPDH primers in bovine liver cDNA
2. Bovine rearranged Cmu heavy chain in bovine brain cDNA from fetus 5996.
3. Bovine rearranged Cmu heavy chain in bovine liver cDNA from fetus 5996.
4. GAPDH primers in bovine spleen cDNA from fetus 5996.
5. Bovine rearranged Cmu heavy chain in bovine spleen cDNA from fetus 5996.
6. GAPDH primers in bovine brain cDNA from fetus 5996.
7. Bovine rearranged Cmu heavy chain positive control.

FIG. 8

1 2 3 4 5 marker 6 7 8 9 10



1. Human rearranged Cmu heavy chain in mouse spleen cDNA with HAC (+ control).
2. Human rearranged Cmu heavy chain in bovine liver cDNA from fetus.
3. Human rearranged Cmu heavy chain in bovine brain cDNA from fetus 5996
4. Human rearranged Cmu heavy chain in human spleen cDNA (+ control).
5. Human rearranged Cmu heavy chain in bovine spleen cDNA from fetus 5996.
6. GAPDH primers in bovine spleen cDNA from fetus 5996.
7. GAPDH primers in mouse spleen cDNA with HAC
8. GAPDH primers in bovine brain cDNA from fetus 5996.
9. GAPDH primers in bovine liver cDNA from fetus 5996.
10. GAPDH primers positive control.

FIG. 9

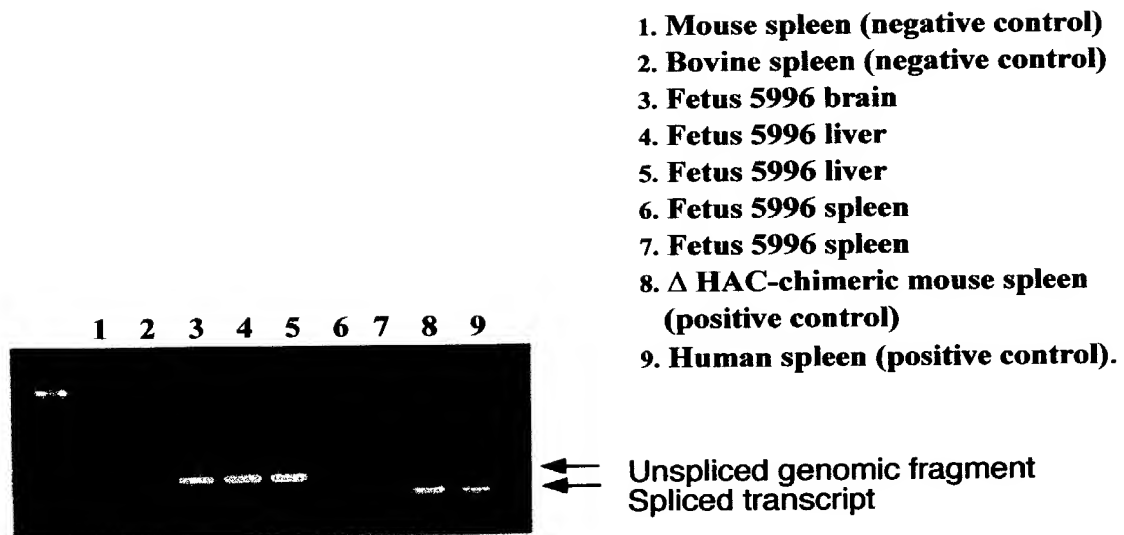
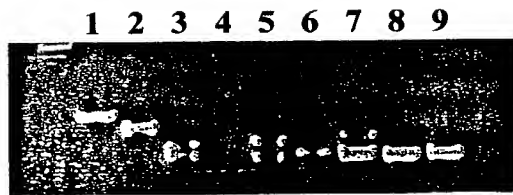


FIG. 10



- 1. Mouse spleen (negative control)**
- 2. Bovine spleen (negative control)**
- 3. Fetus 5996 brain**
- 4. Fetus 5996 liver**
- 5. Fetus 5996 liver**
- 6. Fetus 5996 spleen**
- 7. Fetus 5996 spleen**
- 8. Δ HAC-chimeric mouse spleen (positive control)**
- 9. Human spleen (positive control)**

FIG. 11A

SEQ ID NO: 49

5'

GGGAAGGAAGTCCTGTGCGACCANCCAACGGCCACGCTGCTCGTATCCGACG
 GGGAATTCTCACAGGAGACGAGGGGGGAAAAGGGTTGGGGCGGATGCACTCC
 CTGAGGAGACGGTGACCAGGGTTCNTGGCCCCAGNNGTCAAA3'

FIG. 11B

SEQ ID NOs: 50 and 51

V-D-J region

| → constant mu region

Subject: 5'

tttgactactggggccagggaaccctgggtcacctgtctcctcagggagtgcacccgcccc

-----nn-----n-----

Query

Subject:

acccttttccccctcgtctcctgtgagaattccccgtcggatacgagcagcgtggccgtt

Query

Subject: 5'

ggctgcctcgacaggacttccttcccgaactccatcactttctcctg 3'

--n--g----- Cmul primer

FIG. 12A

SEQ ID NOs: 52 and 53

```

10      19      28      37      46      55
5' GGA GGC TTG GTC AAG CCT GGA GGG TCC CTG AGA CTC TCC TGT GCA GCC TCT GGA
  G G L V K P G G S L R L S C A A S G

64      73      82      91      100      109
TTC ACC TTC AGT GAC TAC TAC ATG AGC TGG ATC CGC CAG GCT CCA GCG AAG GGG
  P T F S D Y Y M S W I R Q A P G K G

118     127     136     145     154     163
CTG GAG TGG GTT TCA TAC ATT AGT AGT AGT AGT ACC ATA TACT AC GCA GAC
  L B W V S Y I S S S G S T I Y Y A D
                                VH3-11

172     181     190     199     208     217
TCT GTG AAG GGCCGA TTC ACC ATC TCC AGG GAC AAC GCC AAG AAC TCA CTG TAT
  S V K G R F T I S R D N A K N S L Y

226     235     244     253     262     271
CTG CAA ATG AAC AGC CTG AGA GCC GAG GAC ACG GCT GTG TAT TAC TGT GCG AGA
  L Q M N S L R A E D T A V Y Y C A R

280     289     298     307     316     325
ATA ACT GGG GAT GCT TTT GAT ATC TGG GGC CAA GGG ACA ATG GTC ACC GTC TCT
  I T G D A F D I W G Q G T M V T V S
                                JH3
D7-27 334     343     352     361     370     379
TCA GGG AGT GCA TCC GCC CCA ACC CTT TTC CCC CTC GTC TCC TGT GAG AAT TCC
  S G S A S A P T L F P L V S C E N S

388
CCG TCG GAT ACG AGC 3'
  P S D T S

Cμ
```

09980115.060602

FIG. 12B

SEQ ID NOs: 54 and 55

5' GTG GAG TCT GGG GGA GGC TTG GTA CAG CCT GGG AGG TCC CTG AGA CTC TCC TGT
V E S G G G L V Q P G R S L R L S C

OCA GCG TCA GGA TTC ACC TTC AGG AAC TTT GGC ATG CAC TGG GTC CGC CAG CCT
A A S G F T F R N F G M H W V R Q A
VH3-33

CCA GGC AAG GGG CTG GAG TGG GTG ACA GTT ATA TGG TAT GAC GGA AGT AAT CAA
P G K G L E W V T V I W Y D G S N Q

TAC TAT ATA GAC TCC GTG AAG GGC CGA TTC ACC ATC TCC AGA GAC AAT TCC AAG
Y Y I D S V K G R F T I S R D N S K

AAC ATG TTG TAT CTG CAA ATG AAC AGC CTG AGA GCC GAG GAT ACG CCT GTG TAT
N M L Y L Q M N S L R A B D T A V Y

TAC TGT GCG AGA GAT CGC AAT GGC CTG AAG TAC TTC GAT CTC TGG GGC CGT GGC
Y C A R D R N G L K Y F D L W G R G
D6-39 ? N addition JH2

ACC CTG GTC ACT GTC TCA TCA GGG AGT GCA TCC GGC CCA ACC CTT TTT C C C C C
T L V T V S S G S A S A P T L F P L

GTC TCC TGT GAG AAT TCC CGG TCG GAT ACG AGC }
V S C E N S P S D T S
Cμ

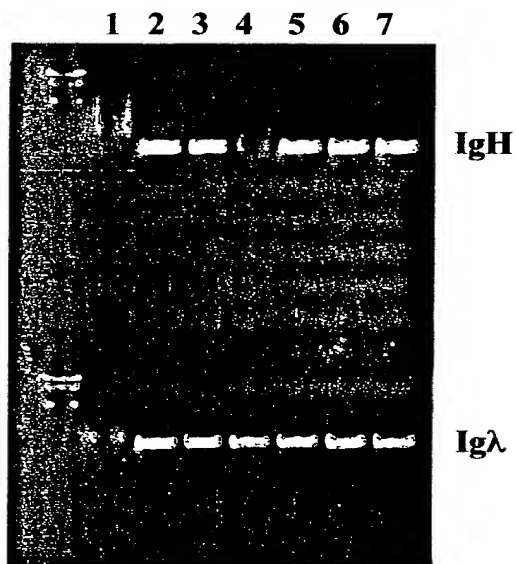
FIG. 13



Fetus	Clone	IgH	Igλ
5580	412	Pos	Pos
5848	214	Neg	Neg

1. Bovine genomic DNA (negative control)
2. Fetus 5580 genomic DNA (Igλ)
3. Fetus 5580 genomic DNA (Igλ)
4. Fetus 5848 genomic DNA (Igλ)
5. Fetus 5848 genomic DNA (Igλ)
6. Positive control (Human genomic DNA)
7. Bovine genomic DNA (negative control)
8. Fetus 5580 genomic DNA (IgH)
9. Fetus 5580 genomic DNA (IgH)
10. Fetus 5848 genomic DNA (IgH)
11. Fetus 5848 genomic DNA (IgH)
12. Positive control (Human genomic DNA)

FIG. 14



IgH

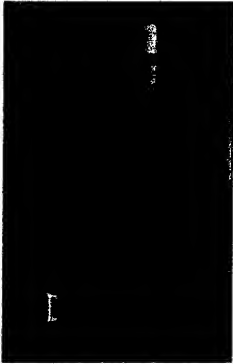
1. Bovine genomic DNA (negative control)
2. Fetus 5442A genomic DNA (91 day)
3. Fetus 5442A genomic DNA (91 day)
4. Fetus 5442B genomic DNA (91 day)
5. Fetus 5442B genomic DNA (91 day)
6. Fetus 5968 genomic DNA (56 day; positive control)
7. Human genomic DNA (positive control)

Igλ

FIG. 15

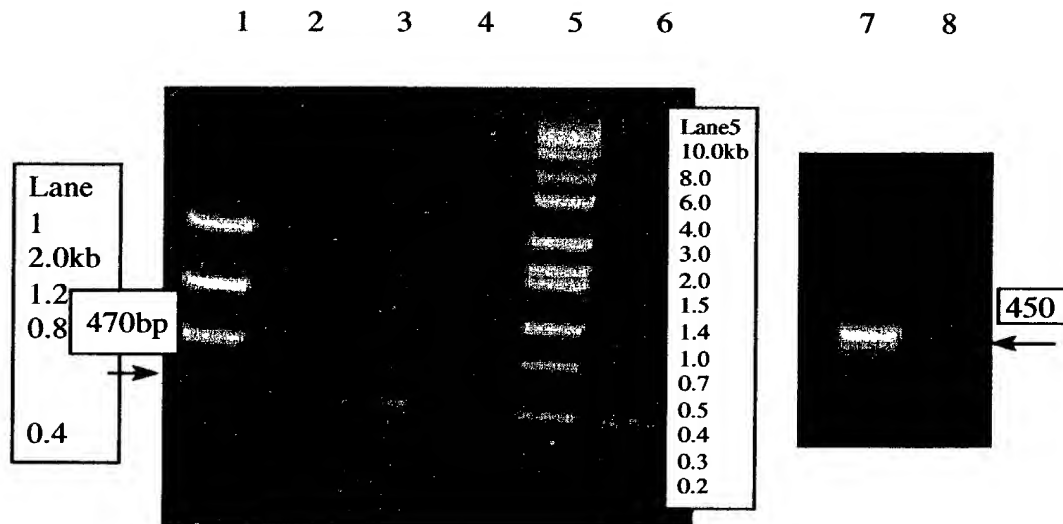
- 1. Bovine spleen (negative control)
- 2. Fetus 5442A brain
- 3. Fetus 5442A liver
- 4. Fetus 5442A spleen
- 5. Fetus 5442A spleen
- 6. Fetus 5996 spleen (positive control)
- 7. ΔHAC-chimeric mouse spleen (positive control)

1 2 3 4 5 6 7



Unspliced genomic fragment
Spliced transcript

FIG. 16



1. Low Mass Ladder: 2.0, 1.2, 0.8, 0.4, 0.2
0.1kb
2. Normal Bovine spleen cDNA negative
3. ΔΔHAC 5868A spleen
4. empty
5. Hi Lo
- 0.2, 0.1kb
6. Tc Mouse HAC spleen cDNA positive
7. GAPDH product from 5868A spleen cDNA
8. GAPDH product from normal bovine
cDNA

FIG. 17

1. Bovine spleen (negative control)
2. Fetus 5442A brain
3. Fetus 5442B brain
4. Fetus 5442A liver
5. Fetus 5442B liver
6. Fetus 5442A spleen
7. Fetus 5442A spleen
8. Fetus 5442B spleen
9. Fetus 5442B spleen
10. Δ HAC-chimeric mouse spleen
(positive control)

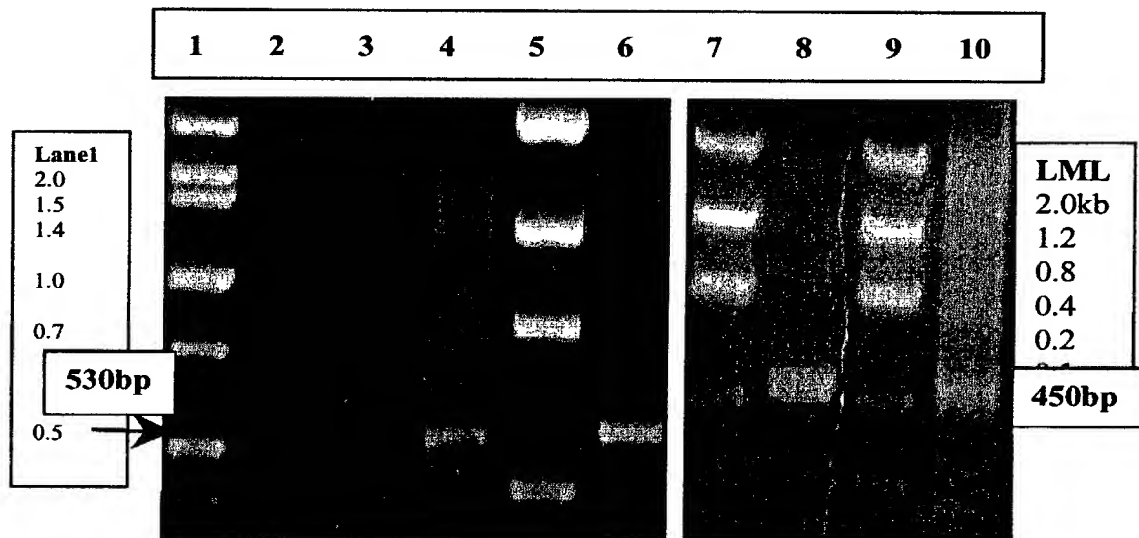


FIG. 18

1. Bovine spleen (negative control)
2. Fetus 5442A brain
3. Fetus 5442A liver
4. Fetus 5442A spleen
5. Fetus 5442A spleen
6. Δ HAC-chimeric mouse spleen
(positive control)



FIG. 19



1. Hi-Lo MW:2.0,1.5,1.4,1.0,0.7,0.5 kb
2. $\Delta\Delta$ HAC 5868A fetal brain cDNA
3. $\Delta\Delta$ HAC 5868A fetal liver cDNA
4. $\Delta\Delta$ HAC 5868A fetal spleen cDNA
5. Low Mass Ladder
6. Tc Mouse HAC spleen cDNA positive control (530bp)
7. Low Mass Ladder
8. GAPDH $\Delta\Delta$ HAC 5868A brain cDNA
9. Low Mass Ladder
10. GAPDH $\Delta\Delta$ HAC 5868A liver cDNA

FIG. 20

SEQ ID NOs: 56 and 57

5' ACC CTC CTC ACT CAC TGT GCA GGG TCC TGG GCC CAG TCT GTG CTG ACT CAG CCA
T L L T H C A G S W A Q S V L T Q P

CCC TCA GCG TCT GGG ACC CCC GGG CAG AGG GTC ACC ATC TCT TGT TCT GGA AGC
P S A S G T P G Q R V T I S C S G S

AGC TCC AAC ATC GGA AGT AAT TAT GTA TAC TGG TAC CAG CAG CTC CCA GGA ACG
S S N I G S N Y V Y W Y Q Q L P G T

GCC CCC AAA CTC CTC ATC TAT AGG AAT AAT CAG CGG CCC TCA GGG GTC CCT GAC V1-17
A P K L L I Y R N N Q R P S G V P D

CGA TTC TCT GGC TCC AAG TCT GGC ACC TCA GCC TCC CTG GCC ATC AGT GGG CTC
R F S G S K S G T S A S L A I S G L

CGG TCC GAG GAT GAG GCT GAT TAT TAC TGT GCA GCA TGG GAT GAC AGC CTG AGT
R S E D E A D Y Y C A A W D D S L S

GGT CTT TTC GGC GGA GGG ACC AAG CTG ACC GTC CTA GGT CAG CCC AAG GCT GCC
G L F G G G T K L T V L G Q P K A A

CCC TCG GTC ACT CTG TTC CCA CCC TCC TCT GAG GAG CTT CAA GCC AAC AAG GCC
P S V T L F P P S S E E L Q A N K A

ACA CTG GTG 3' Ca
T L V

FIG. 21

SEQ ID NOs: 58 and 59

5' AGT TGG ACC CCT CTC TGG CTC ACT CTC TTC ACT CTT TGC ATA GGT TCT
S W T P L W L T L F T L C I G S

GTG GTT TCT TCT GAG CTG ACT CAG GAC CCT GCT GTG TCT GTG GCC TTG GGA CAG
V V S S E L T Q D P A V S V A L G Q

ACA GTC AGG ATC ACA TGC CAA GGA GAC AGC CTC AGA AGC TAT TAT GCA AGC TGG
T V R I T C Q Q G D S L R S Y Y A S W

TACCAGCAG AAG CCA GGA CAG GCC CCT GTA CTT GTC ATC TAT GGT AAA AAC AAC V2-13
Y Q Q K P G Q A P V L V I Y G K N N

CGG CCC TCA GGG ATC CCA GAC CGA TTC TCT GGCTCC AGC TCA GGA AAC ACA GCT
R P S G I P D R F S G S S G N T A

TCC TTG ACC ATC ACT GGG GCT CAG GCG GAA GAT GAG GCT GAC TAT TAC TGT AAC
S L T I T G A Q A E D E A D Y Y C N

TCC CGG GAC AGC AGT GGT AAC CAT CTG GTA TTC GGC GGA GGG ACC AAG CTG ACC
S R D S S G N H L V F G G G T K L T JL2

GTC CTA GGT CAG CCC AAG GCT GCC CCC TCG GTC ACT CTG TTC CCA CCC TCC TCT
V L G Q P K A A P S V T L F P P S S

GAG GAG CTT CAA GCC AAC AAG GCC ACA CTG GTG 3'
E E L Q A N K A T L V

Ca

09950115 . 060002

FIG. 22A

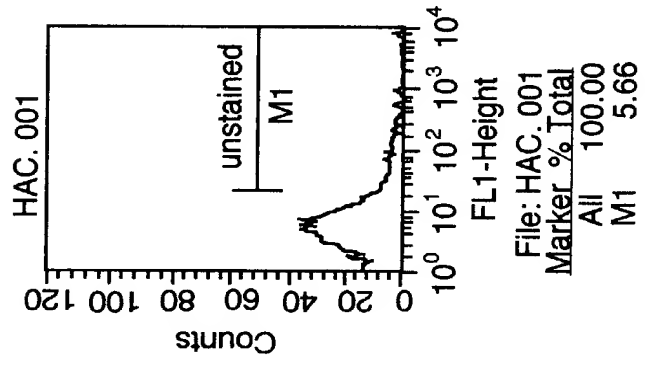


FIG. 22B

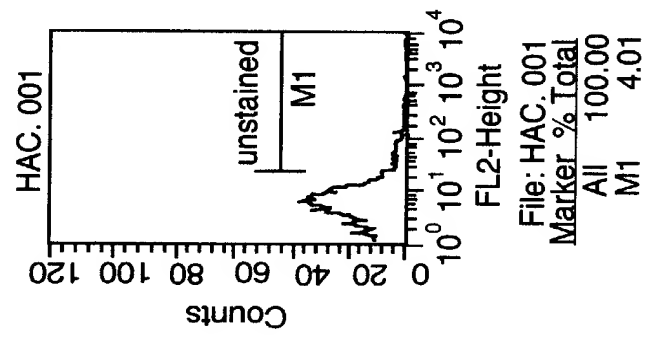


FIG. 22C

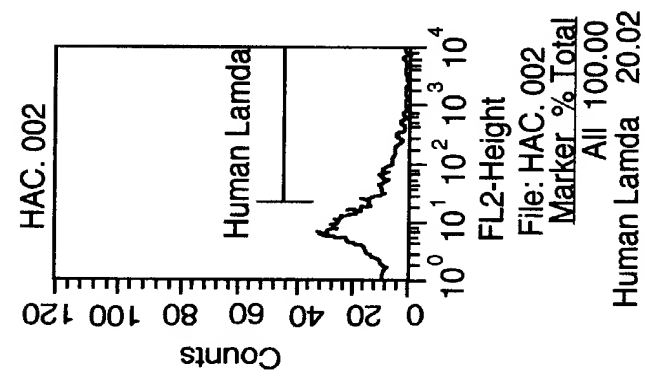


FIG. 22D

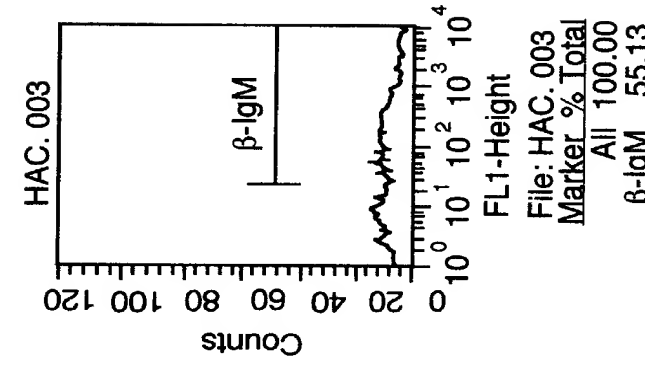


FIG. 22E

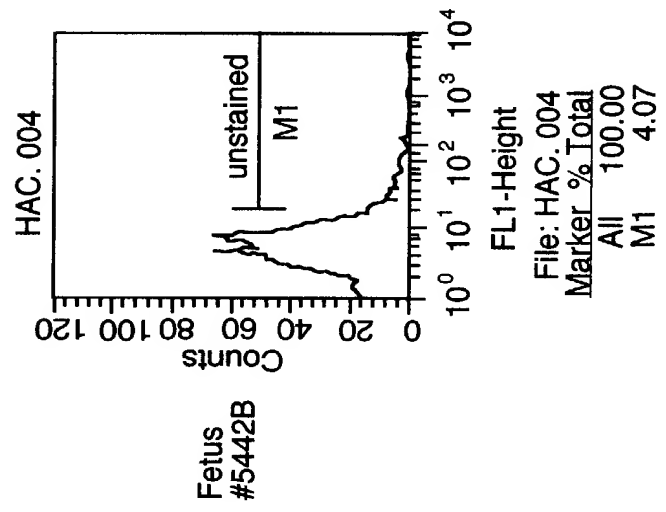


FIG. 22F

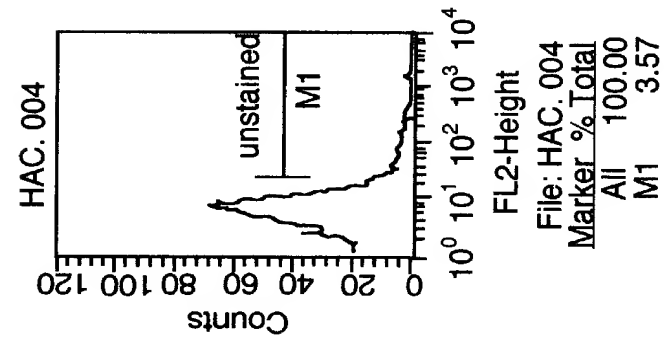


FIG. 22G

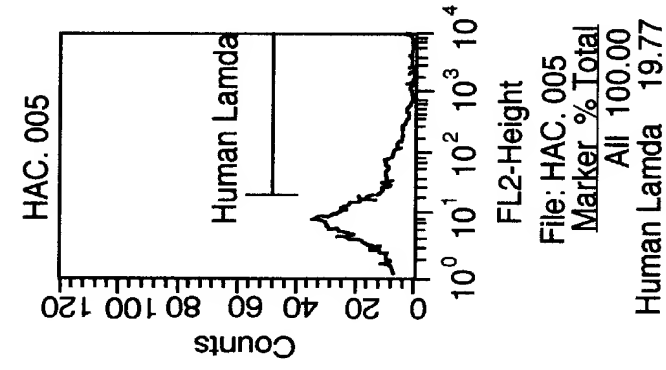


FIG. 22H

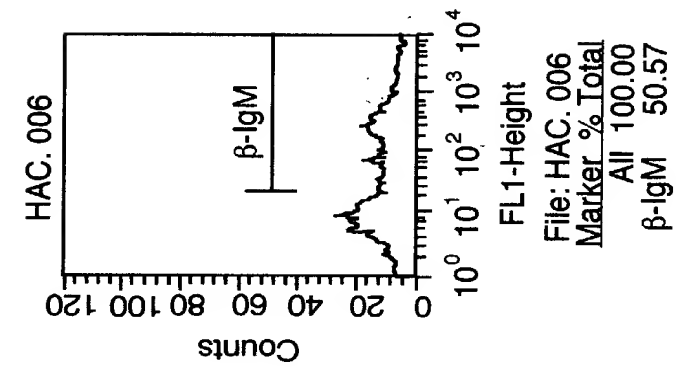


FIG. 23

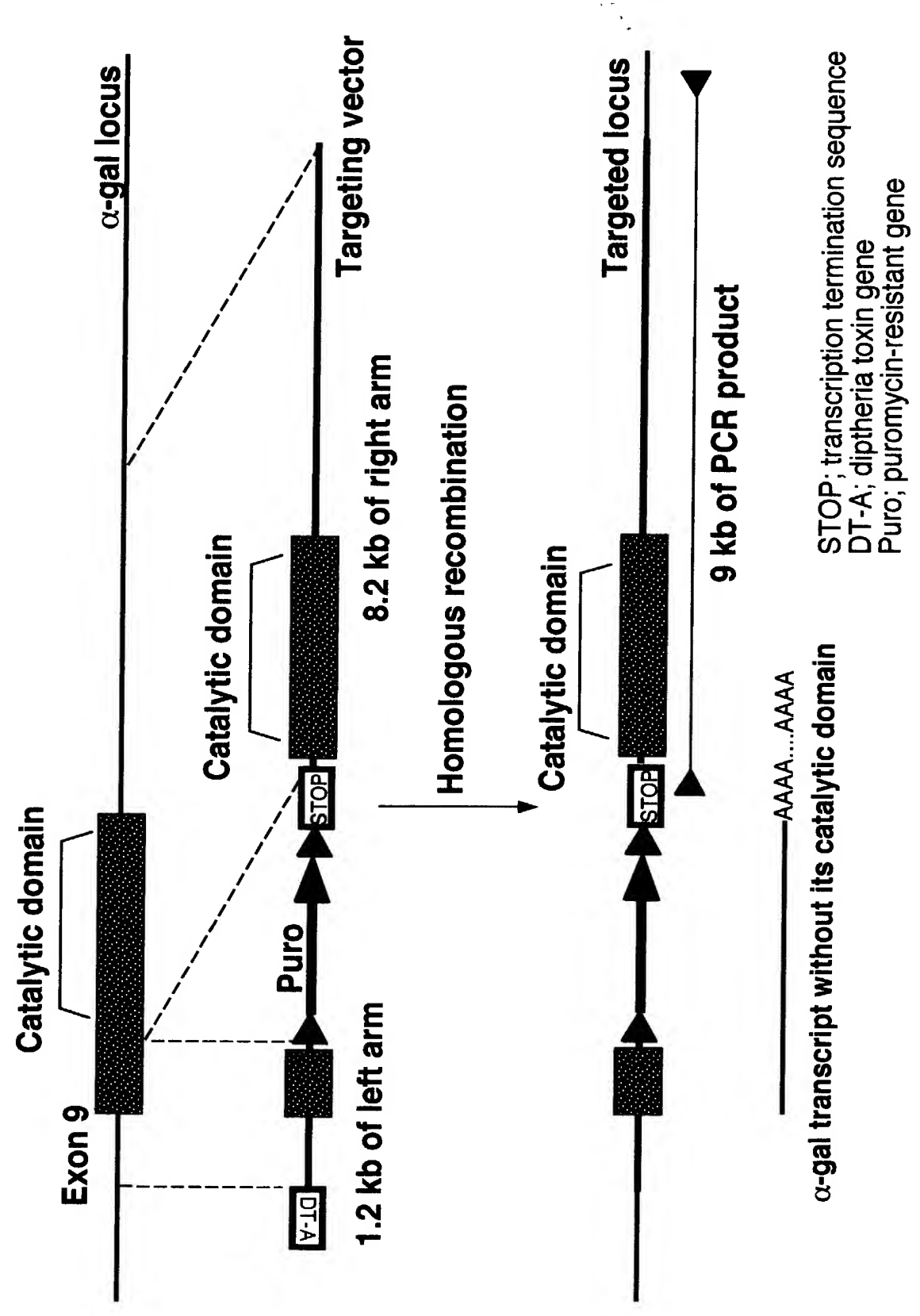


FIG. 24

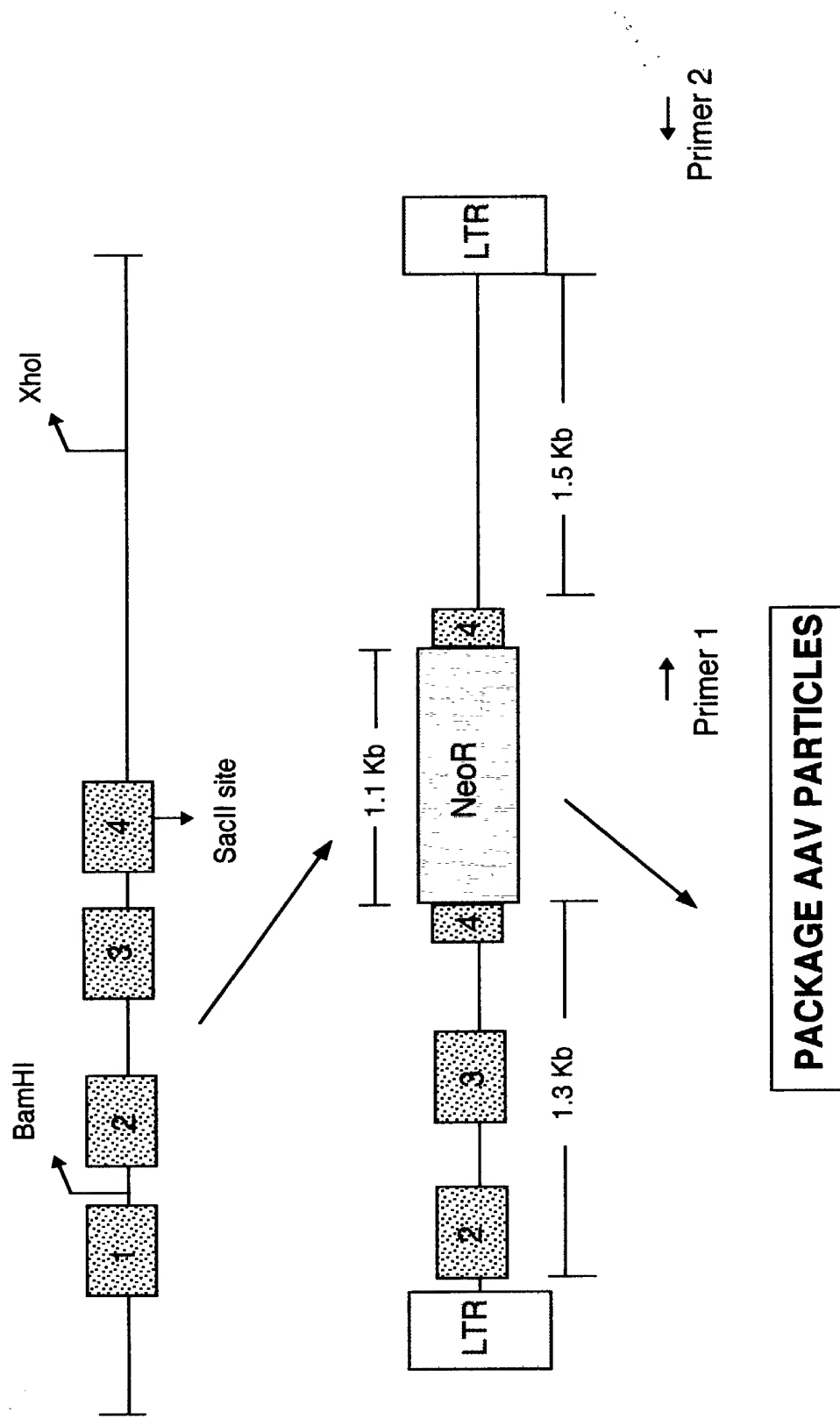
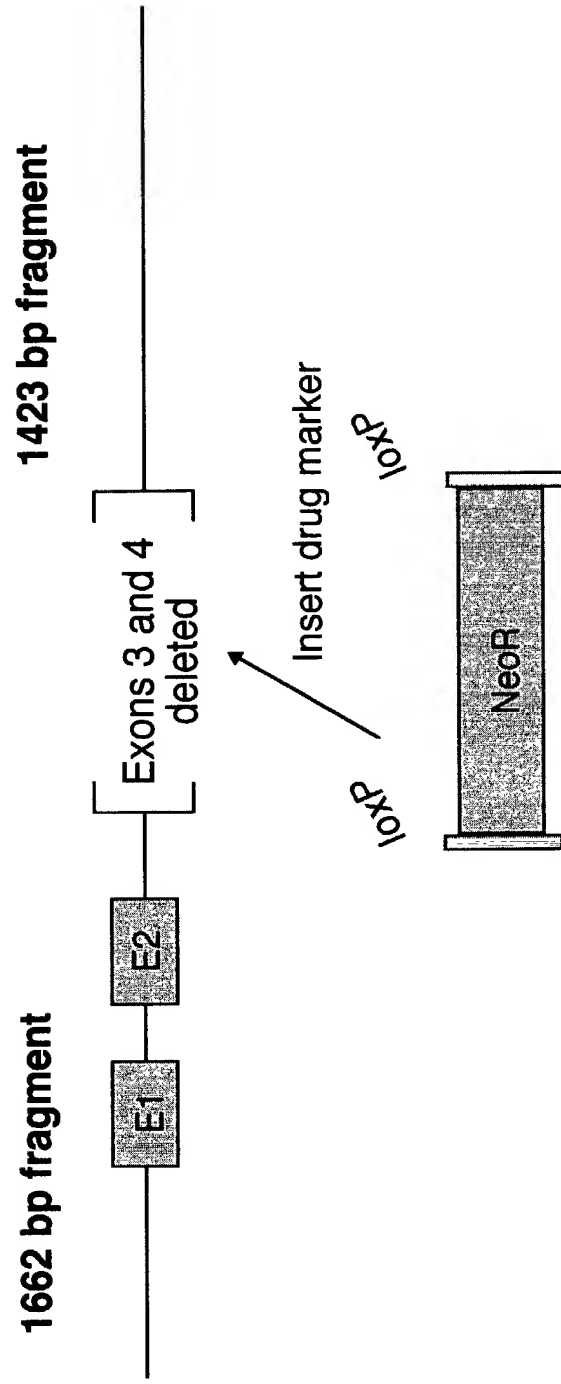


FIG. 25



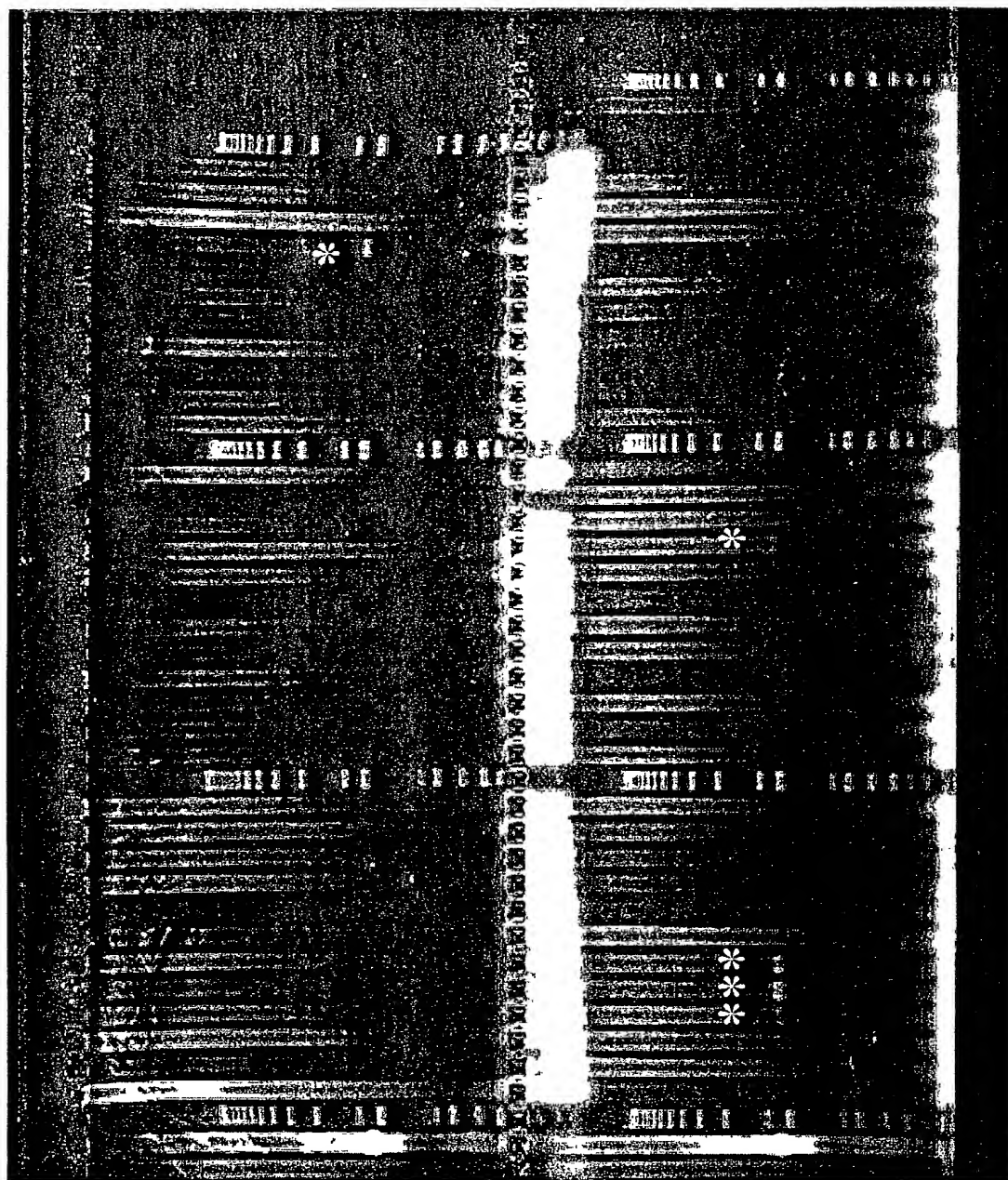


FIG. 26

FIG. 27

NT, ET and pregnancies :Delta HAC regenerated fibroblasts												
Cell line	Total NTs	No of Blast	No of Blast	Pregnancy status								
ID	In culture	(%)	Transferred	No Recips	40 d	60 d	90 d	120 d	150 d	180 d	210 d	
D5968	174	34 (28)	27	17	3	3	3	3	3	3	3	3
D6045	215	10 (7)	8	4	1	1	1	1	1	1	1	
D6045	122	20 (23)	12	9	1	0	0	0	0	0	0	
D6032	161	18 (16)	14	7	3	3	3	2	2	2		
D6032	188	15 (11)	11	11	3	0	0	0	0	0		
D6032	198	20 (14)	16	10	1	1	1	1				
D6032	200	17 (12)	12	8	2	2	2	2				
D6032	180	11 (9)	10	5	3	1	1	0				
D6032	135	22 (23)	22	11	2	1	1	1				
D5968	140	35 (36)	25	13	2	2	1					
D5968	180	30 (24)	26	13	2	2	1					
D6045	170	46 (39)	32	16	4							
D6045	80	7 (13)	1	1	0							
D6045 SLOT	108	9 (12)	3	2	1							
D6045	76	8 (15)	2	1	0							
D6045 SLOT	128	12 (13)	7	5	0							
D6045	47	6 (18)	5	3	2							
D6045 SLOT	112	3 (4)	3	2	2							
D6045	120	28 (33)	18	9								
D6045 SLOT	100	11 (16)	2	1								
D6045	78	15 (27)	16	8								
D6045 SLOT	91	0	2	1								
D6045	98	16 (23)	10	5								
D6045 SLOT	104	16 (22)	10	5								
D5968	128	24 (27)	8	4								
D5968 SLOT	65	10 (22)	8	4								
D5968	120	28 (33)	14	7								
D5968 SLOT	95	13 (19)	6	3								
D5968	98	17 (25)	20	10								
D5968 SLOT	93	14 (22)	12	6								
D	13	1 (11)	1	3								
SLOT	63	8 (18)	8	3								
D	108	4 (5)	4	3								
SLOT	100	1 (1)	1	3								
D	90	10 (16)	10	6								
SLOT	110	13 (17)	13	6								
D	90	10 (16)	10	1								
SLOT	83	5 (9)	5	1								
D	105	20 (27)	20	9								
SLOT	78	7 (13)	7	2								
D	88	7 (11)	7	4								
SLOT	93	9 (14)	9	4								
D	85	20 (33)	20	10								
SLOT	77	4 (7)	4	2								
	4967	515 (19)	481	258								

Summary	
Preg Status	No of Pregnancies
> 40 d	9
> 90 d	2
> 120 d	4
> 180 d	3
> 210 d	3
Total	21